

Amendment to the CLAIMS

Claims

1. (currently amended) A [[M]]mammalian cell comprising:
 - a] a first side comprising a functional hNTCP protein; and
 - b] a second side comprising a functional hBSEP protein

~~having a first and a second side which both sides form part of the outer surface of such cell and which both sides are different from the areas of contact of such cell and which first and second side~~ wherein the first side is ~~are~~ distinguished from the second side by each other by ~~their localization at opposite ends of such said cell wherein the first side carries a functional hNTCP protein and the second side carries a functional hBSEP protein.~~
2. (currently amended) ~~Mammalian cell as claimed in claim 1~~ The mammalian cell according to claim 1 wherein the first side is the basolateral side and the second side is the apical side.
3. (canceled)
4. (currently amended) ~~Mammalian cell as claimed in claim 1 to 3~~ The mammalian cell according to claim 1 wherein the cell is an epithelial cell of an organ or a system wherein the organ or the system is selected from the group consisting of ~~the kidney, of the bowels system, of the liver and or of the blood/brain barrier.~~
5. (currently amended) ~~Mammalian cell as claimed in claims 1 to 4 which~~ The mammalian cell according to claim 1 wherein the cell is immortalized.
6. (currently amended) ~~Mammalian cell as claimed in claims 1 to 5 which~~ The mammalian cell according to claim 1 wherein the cell is a recombinant cell.
7. (currently amended) ~~Mammalian cell as claimed in claims 1 to 6 which~~ The mammalian cell according to claim 1 wherein the cell is a LLC-PK1 cell comprising one or more vector(s) ~~harboring a vector~~ for expressing the hNTCP protein and ~~a vector for expressing the~~ hBSEP protein.

8. (currently amended) ~~Mammalian cell as claimed in claims 1 to 6 which~~ The mammalian cell according to claim 1 wherein the cell is a MDCKII cell comprising one or more vector(s) harboring a vector for expressing the hNTCP protein and a vector for expressing the hBSEP protein.
9. (currently amended) ~~Mammalian cell as claimed in claim 8 according to~~ The mammalian cell according to claim 1 wherein the cell is deposit DSM ACC2643 or progeny thereof.
10. (currently amended) A method of manufacturing a mammalian cell according to claim 1 comprising: Manufacturing of a mammalian cell according to claims 1 to 9 wherein
a) providing a mammalian cell ~~is provided~~;
b) providing a vector ~~is provided encompassing~~ comprising the coding sequence of hNTCP;
c) providing a vector ~~is provided encompassing~~ comprising the coding sequence of hBSEP;
d) transforming the mammalian cell from a) ~~is transformed~~ by a vector from b) and by a vector from c) either simultaneously or consecutively;
e) identifying and propagating a double transfectant cell from d) ~~is identified and propagated~~.
11. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claim 10~~ The method of claim 10 wherein the mammalian cell from a) is an epithelial cell of an organ or a system wherein the organ or the system is selected from the group consisting of the kidney, of the bowels system, of the liver and or of the blood/brain barrier.
12. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 10 and 11~~ The method of claim 10 wherein the mammalian cell from a) is immortalized.
13. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 10 to 12~~ The method of claim 10 wherein the vector from b) is a polynucleotide according to Fig.9 (Seq ID No. 4).
14. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 10 to 12~~ The method of claim 10 wherein the vector from c) is a polynucleotide according to Fig. 10 (Seq ID No. 5).

15. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 10 to 14~~ The method of claim 10 wherein the mammalian cell ~~is build up as~~ comprises deposited cell DSM ACC2643 or the progeny thereof.
16. (currently amended) A monolayer of cells comprising at least two cells according to ~~claims 1 to 9~~ claim 1.
17. (currently amended) ~~The monolayer of cells~~ A solid surface carrying a monolayer according to claim 16 wherein the monolayer of cells ~~could occupy the part or the whole of the~~ a solid surface.
18. (currently amended) ~~The [[A]] solid surface as claimed in~~ according to claim 17 wherein the solid surface comprises ~~that is formed by~~ a plastic.
19. (currently amended) ~~The [[A]] solid surface as claimed in~~ according to claim 17 wherein the solid surface comprises ~~that is part of~~ a petri dish.
20. (currently amended) ~~The [[A]] solid surface as claimed in~~ according to claim 17 wherein the solid surface comprises ~~that is part of a filter insert~~ a filter membrane.
21. (currently amended) A petri dish carrying a monolayer of cells according to claim ~~17~~ 20.
22. (currently amended) ~~The filter membrane~~ A filter insert carrying a monolayer of cells according to claim ~~17~~ 20 wherein the filter membrane comprises a filter-insert.
23. (currently amended) ~~The [[A]] filter-insert as claimed in~~ according to claim 22 wherein the filter membrane support is made of comprises polycarbonate ~~and/or~~ or polyester.
24. (currently amended) ~~The [[A]] filter-insert~~ according to claim 22 ~~as claimed in claims 22 and 23~~ wherein the filter membrane support's has a pore size is of 0.4 µm.
25. (currently amended) ~~A method~~ Use of a mammalian cell of claims 1 to 9 for determining a pharmacological profile comprising:
- a) providing a monolayer of cells according to claim 16;

- b] adding a labeled compound to a first compartment of the monolayer;
c] incubating the labeled compound with the monolayer;
d] measuring the amount of the labeled compound in the first compartment of the monolayer and in a second compartment of the monolayer; and
e] comparing the amount of the labeled compound in the first compartment to the second compartment to determine a difference
thereby identifying the pharmacological profile wherein the pharmacological profile is selected from the group consisting of with respect to hepatobiliary elimination, and/or renal excretion, and/or brain resorption and/or and intestinal resorption.
26. (currently amended) The method according to Use of a mammalian cell as claimed in claim 25 wherein the mammalian cell forms part of a monolayer on a solid surface wherein the solid surface is selected from the group consisting of and/or on a petri dish, and/or on a filter membrane and a filter-insert.
27. (currently amended) A [[M]]mammalian cell comprising:
a] a first side comprising a functional hNTCP protein; and
b] a second side comprising a functional hBSEP protein
~~having a first and a second side which both sides form part of the outer surface of such cell and which both sides are different from the areas of contact of such cell and which first and second side wherein the first side is are distinguished from the second side by each other by their localization at of opposite ends of such said cell wherein the first side carries a functional hNTCP protein and the second side carries a functional hMRP2 protein.~~
28. (currently amended) ~~Mammalian cell as claimed in claim 27~~ The mammalian cell according to claim 27 wherein the first side is the basolateral side and the second side is the apical side.
29. (canceled)
30. (currently amended) ~~Mammalian cell as claimed in claims 27 to 29~~ The mammalian cell according to claim 27 wherein the cell is an epithelial cell of an organ or a system wherein the organ or the system is selected from the group consisting of kidney, of the bowels system, of the liver and or of the blood/brain barrier.

31. (currently amended) ~~Mammalian cell as claimed in claims 27 to 30 which~~ The mammalian cell according to claim 27 wherein the cell is immortalized.
32. (currently amended) ~~Mammalian cell as claimed in claims 27 to 31 which~~ The mammalian cell according to claim 27 wherein the cell is a recombinant cell.
33. (currently amended) ~~Mammalian cell as claimed in claims 27 to 32 which~~ The mammalian cell according to claim 27 wherein the cell is a LLC-PK1 cell comprising one or more vector(s) harboring a vector for expressing the hNTCP protein and a vector for expressing the hMRP2 protein.
34. (currently amended) ~~Mammalian cell as claimed in claims 27 to 33 which~~ The mammalian cell according to claim 27 wherein the cell is a MDCKII cell comprising one or more vector(s) harboring a vector for expressing the hNTCP protein and a vector for expressing the hMRP2 protein.
35. (currently amended) ~~Mammalian cell as claimed in claims 27 to 34 as~~ The mammalian cell according to claim 27 wherein the cell is deposited as DSM ACC2644 or progeny thereof.
36. (currently amended) A method of manufacturing a mammalian cell according to claim 27 comprising: Manufacturing of a mammalian cell according to claims 27 to 35 wherein
- a] providing a mammalian cell ~~is provided;~~
 - b] providing a vector ~~is provided encompassing~~ comprising the coding sequence of hNTCP;
 - c] providing a vector ~~is provided encompassing~~ comprising the coding sequence of hMRP2;
 - d] transforming the mammalian cell from a] ~~is transformed~~ by a vector from b] and by a vector from c] either simultaneously or consecutively;
 - e] identifying and propagating a double transfectant cell from d] ~~is identified and propagated.~~
37. (currently amended) ~~Manufacturing of a mammalian cell as claimed in~~ The method of claim 36 wherein the mammalian cell from a] is an epithelial cell of an organ or a system wherein the organ or the system is selected from the group consisting of the kidney, of the bowels system, of the liver or of the and blood/brain barrier.

38. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 36 and 37~~ The method of claim 36 wherein the mammalian cell from a] is immortalized.
39. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 36 to 38~~ The method of claim 36 wherein the vector from b] is a polynucleotide according to Fig. 9 (Seq ID No. 4).
40. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 36 to 38~~ The method of claim 36 wherein the the vector from c] is a polynucleotide according to Fig. 11 (Seq ID No. 6).
41. (currently amended) ~~Manufacturing of a mammalian cell as claimed in claims 36 to 38~~ The method of claim 36 wherein the mammalian cell ~~is build up as~~ comprises deposited cell DSM ACC2644 or the progeny thereof.
42. (currently amended) A monolayer of cells comprising at least two cells according to ~~claims 27 to 35~~ claim 36.
43. (currently amended) ~~The monolayer of cells~~ A solid surface carrying a monolayer according to claim 42 wherein the monolayer of cells ~~could~~ occupy the part or the whole of ~~the~~ a solid surface.
44. (currently amended) The [[A]] solid surface as claimed in according to claim 43 wherein the solid surface comprises ~~that is formed by~~ a plastic.
45. (currently amended) The [[A]] solid surface as claimed in according to claim 43 wherein the solid surface comprises ~~that is part of~~ a petri dish.
46. (currently amended) The [[A]] solid surface as claimed in according to claim 43 wherein the solid surface comprises a filter membrane ~~that is part of a filter insert~~.
47. (currently amended) A petri dish carrying a monolayer of cells according to ~~claims 27 to 35~~ claim 46.

48. (currently amended) The filter membrane ~~A filter insert carrying a monolayer of cells~~ according to ~~claims 27 to 35~~ claim 46 wherein the filter membrane comprises a filter-insert.
49. (currently amended) The [[A]] filter-insert ~~as claimed in~~ according to claim 48 wherein the filter membrane support is made of comprises polycarbonate and/or polyester.
50. (currently amended) The [[A]] filter-insert ~~as claimed in~~ according to claim 48 wherein the filter membrane support's has a pore size is of 0.4 μm .
51. (currently amended) A method ~~Use of a mammalian cell of claims 27 to 35~~ for determining a pharmacological profile comprising:
- a] providing a monolayer of cells according to claim 42;
 - b] adding a labeled compound to a first compartment of the monolayer;
 - c] incubating the labeled compound with the monolayer;
 - d] measuring the amount of the labeled compound in the first compartment of the monolayer and in a second compartment of the monolayer; and
 - e] comparing the amount of the labeled compound in the first compartment to the second compartment to determine a difference
- thereby identifying the pharmacological profile wherein the pharmacological profile is selected from the group consisting of ~~with respect to~~ hepatobiliary elimination, ~~and/or~~ renal excretion, ~~and/or~~ brain resorption ~~and/or~~ and intestinal resorption.
52. (currently amended) The method according to ~~Use of a mammalian cell as claimed in~~ claim 51 wherein the mammalian cell forms part of a monolayer on a solid surface wherein the solid surface is selected from the group consisting of ~~and/or on~~ a petri dish, a filter membrane and ~~and/or on~~ a filter-insert.